Independent Study Title	Beneficial Effects of Melatonin on Post Traumatic Stress Disorder after Spinal Cord Injury Study in Experimental Animal Models
Author	Pawarisa Sapprasert
Degree	Master of Science (Anti-aging and Regenerative Medicine)
Advisor	Lecturer Jarasphol Rintra, M. D.
Co-Advisor	Asst. Prof. Dr. Nopporn Jongkamonwiwat

ABSTRACT

Spinal cord injury (SCI) produces an inflammatory response in the CNS, leading to prolong stress involved HPA axis, stress-related psychopathologics such as post traumatic stress disorder (PTSD). It might play a key role in the down regulation of neurogenesis in adult brain. Whereas anti-inflammatory treatments could prevent this effect, Melatonin is a powerful antioxidant that can cross cell membrane and blood brain barrier (Reiter, Manchester & Tan, 2010). Antioxidants are reported to play an essential role in the survival of neuronal cells and it could also influence the production of new cells (Ott, Gogvadze, Orrenius & Zhivotovsky, 2007).

This research study concentrated in the therapeutic effects of melatonin against post traumatic stress disorder (PTSD) after spinal cord injury that induced by crush SCI in animals model. Female mice (3 months old) are randomly assignment to three different groups of animals; control group, SCI, and SCI+Melatonin. To study of post traumatic stress disorder (PTSD), induction of SCI will perform following the standardized severe crush method briefly, mice will be anesthetized and a laminectomy will perform at the T12. Using Dumont forceps to compress the cord laterally from the sides for 5 sec made crush injury model as previously described by Krityakiarana et al. (2010). For melatonin

treated mice, melatonin (10 mg/kg b.w./day) will deliver by intra-peritoneal injection for 14 days after SCI induction. After 14 days mice were sacrificed and brain tissue was removed for the histochemical procedures study for numbers of newly generated cells, GFAP and Ki-67 use for labeling the newly glial cells. Appropriated statistical analysis use to compare the effects of melatonin among groups.

The fact that reduction in inflammation were achieved via an anti-inflammatory effect of melatonin induction as seen in our study, the number of GFAP-positive cell was decreased in SCI-M group (107 $\pm$ 67.8) comparing with SCI group (175.8 $\pm$ 71.5) without reaching significance ($p = 0.747$) even though, it is not possible to claim that melatonin was responsible for the lack of effect so, dose dependent manner of melatonin and more sample size is necessary for future studies to evaluate the anti-inflammatory effects of melatonin on SCI model.

In our study, significantly difference of slightly gliogenesis, represent in Ki-67 labeling, was seen in hippocampus of SCI-M group (16.25 $\pm$ 12.2) comparing with SCI group (49.8 $\pm$ 26.4) ($p < 0.001$). These results can be confirm the neuroregenerative effect of melatonin do not seem to express in the hippocampus of SCI animal. Moreover, neuroprotective effect may exert around the traumatic lesion of spinal cord as derive from the study of melatonin effect on the functional recovery from SCI animal (Schiaveto-de-Souza, da-Silva, Defino & Del Bel, 2013). Finally, the dose response relationship studies for melatonin and large sample size could promise better results.

Keywords: Gliogenesis/Spinal Cord Injury/PTSD/melatonin